

# ORION GENOMICS®

the *SECOND CODE* biomarker company



# Company Overview

## *Overview:*

- Cancer diagnostics company
- Commercialize products, services and technologies
- Specialize in epigenetics

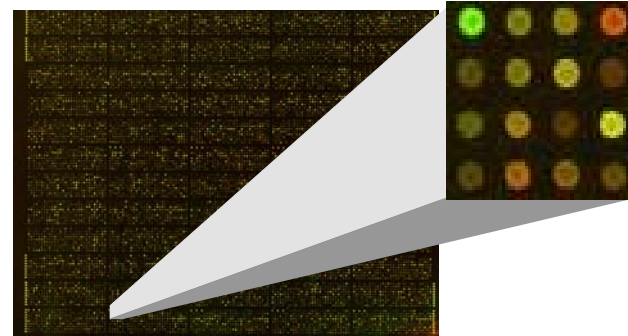
## *Product Pipeline*

- Discovery of 150 new cancer biomarkers
- Validation in 950 patient samples
- Allowed patent for biomarker discovery platform

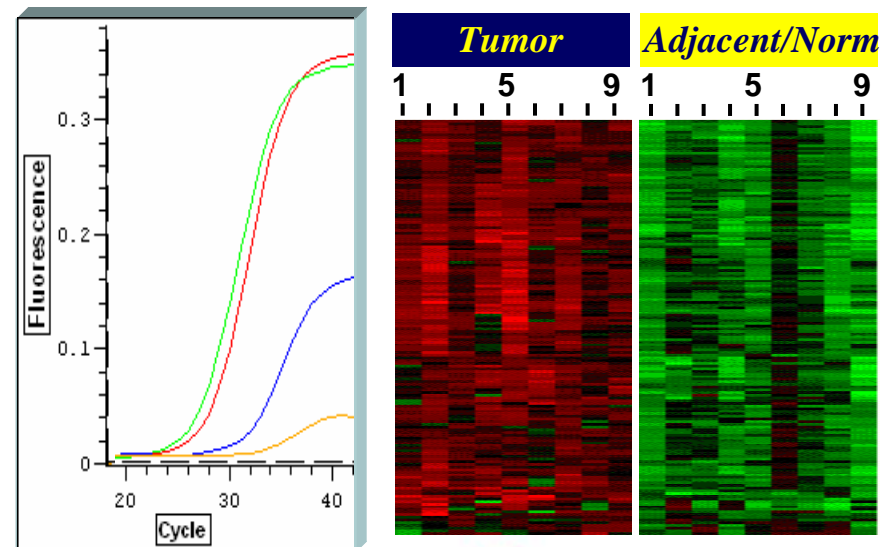
## *Market Opportunity*

- High demand for risk and early detection tests
- Products address large populations

## Genome Wide Biomarker Discovery

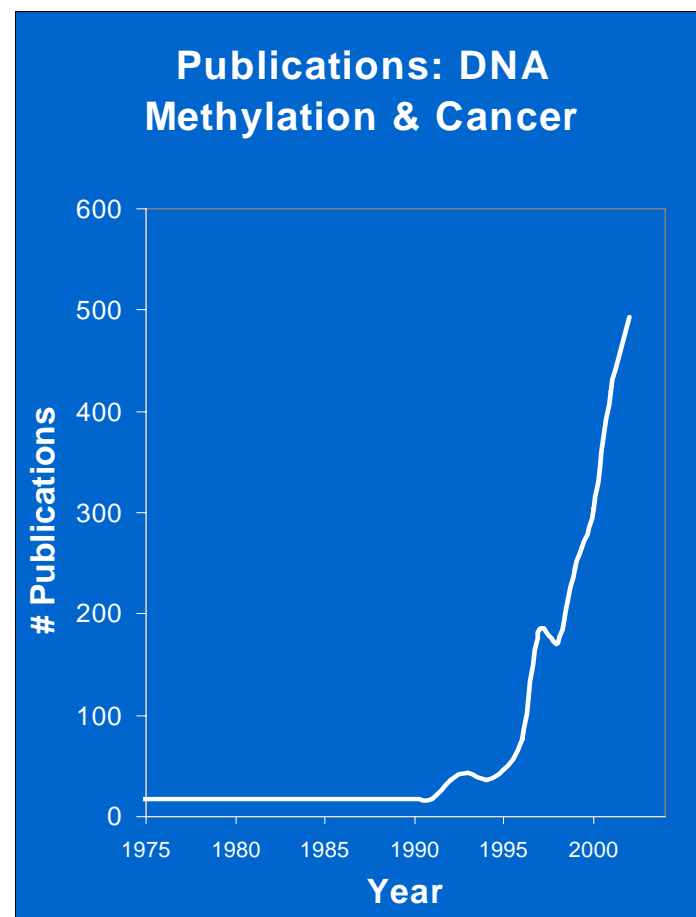


## Clinical Validation



# DNA Methylation & Cancer

- *Cancer is a disease of the genome*
- *DNA methylation codes for chromosomal packaging*
- *Errors in DNA methylation lead to incorrect silencing or activation of genes*
- *DNA methylation biomarkers are strongly linked to cancer*
  - > 4,000 publications
  - Found in every tumor!
  - Linked to tumor progression
  - Linked chemotherapy response
  - Tumor DNA found in serum cancer patients

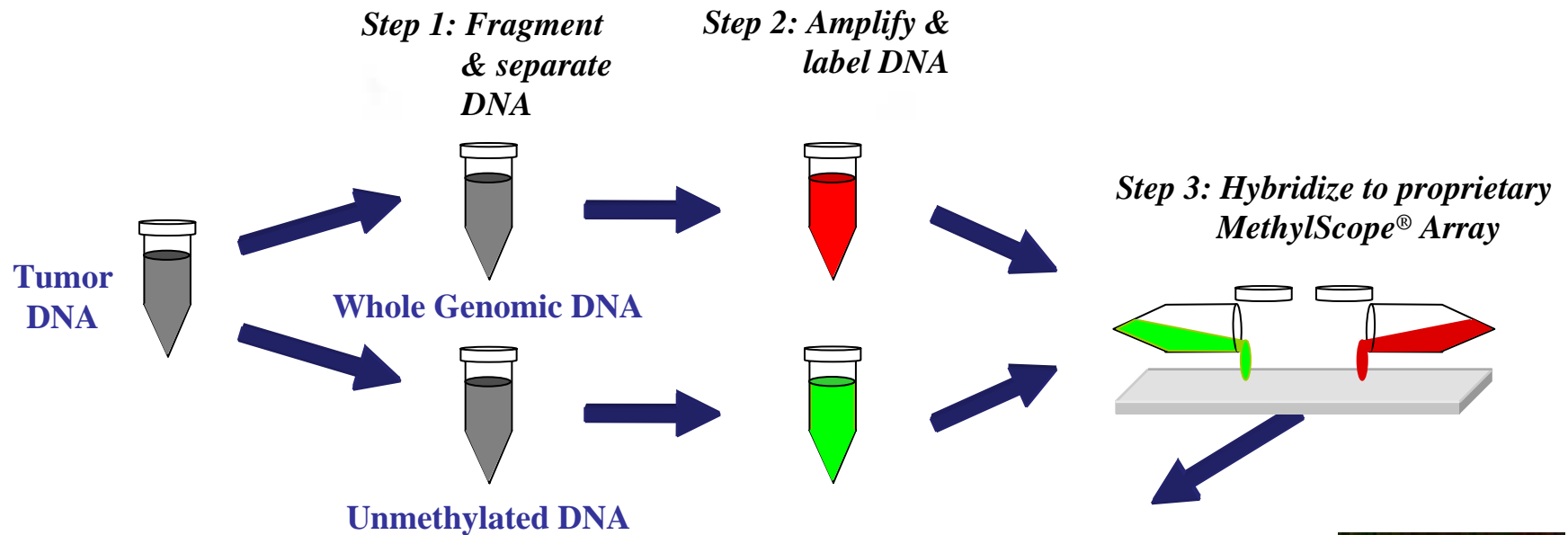


# *MethylScope Technology*

*Simultaneously measuring DNA methylation at 300,000 loci*

# Biomarker Discovery

## MethylScope Technology®

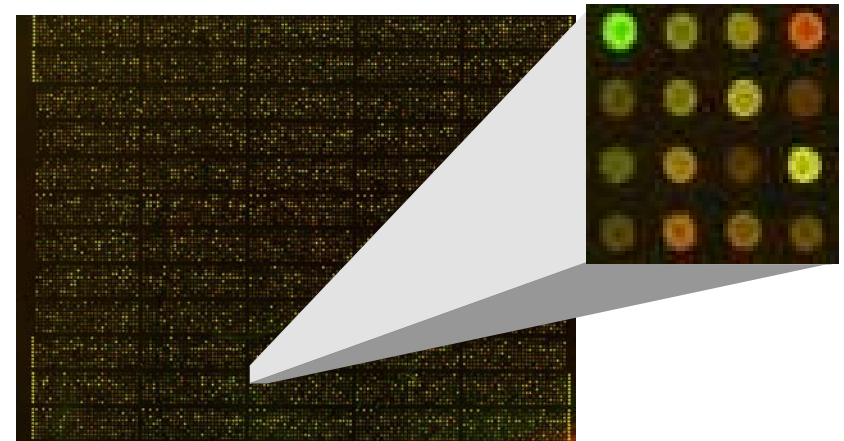


- **Over 400 array hybridizations**
- **5 different tumor types**
- **Array targets all human genes**

*Nature* 430, 471 - 476 (2004)

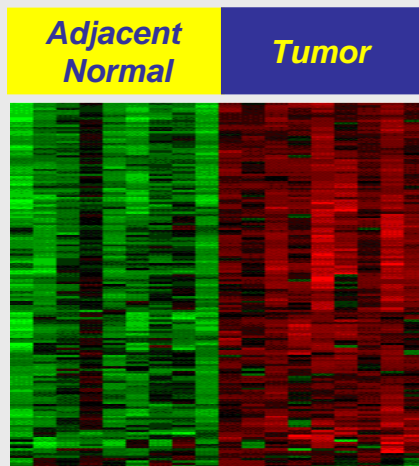
*Nature Methods* 2, 219 - 224 (2005)

*Carcinogenesis* (04 Sep 2006)



# Discovery of High Frequency DNA Methylation Changes in Cancer

## Breast Cancer

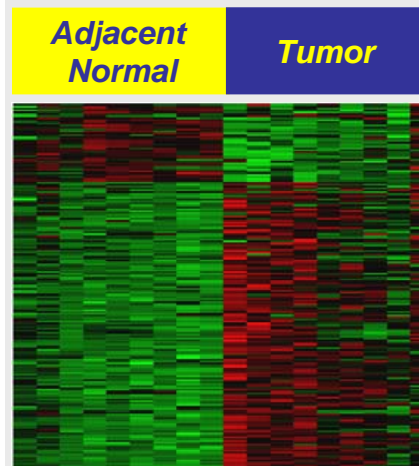


**Specimen Profiled:**

- 9 tumors
- 9 adj. normal

**220 Biomarkers**

## Lung Cancer

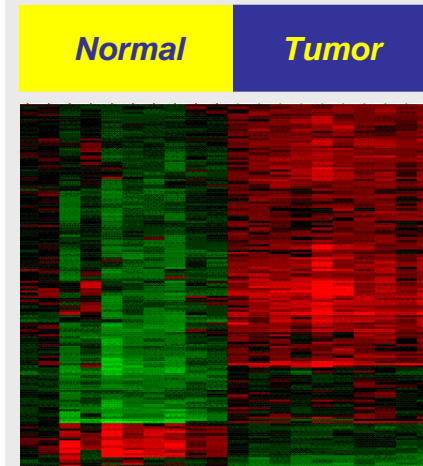


**Specimen Profiled:**

- 9 tumors
- 9 adj. normal

**192 Biomarkers**

## Ovarian Cancer



**Specimen Profiled:**

- 9 tumors
- 9 adj. normal

**151 Biomarkers**



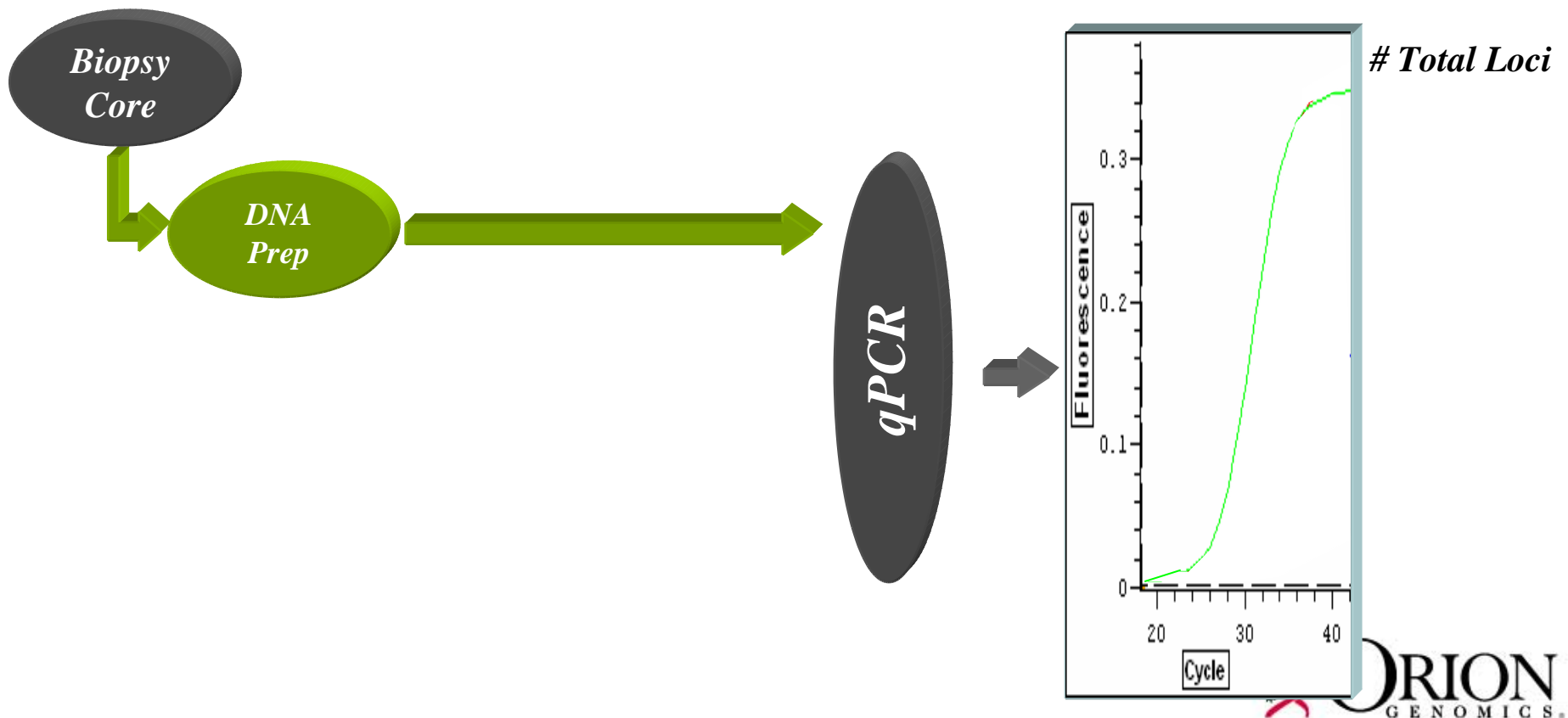
# *MethylScreen Technology*

*Sensitively measuring DNA methylation at a single locus...*

# MethylScreen™ Assay

A straight forward assay:

- *Starts with DNA from a biopsy core...*

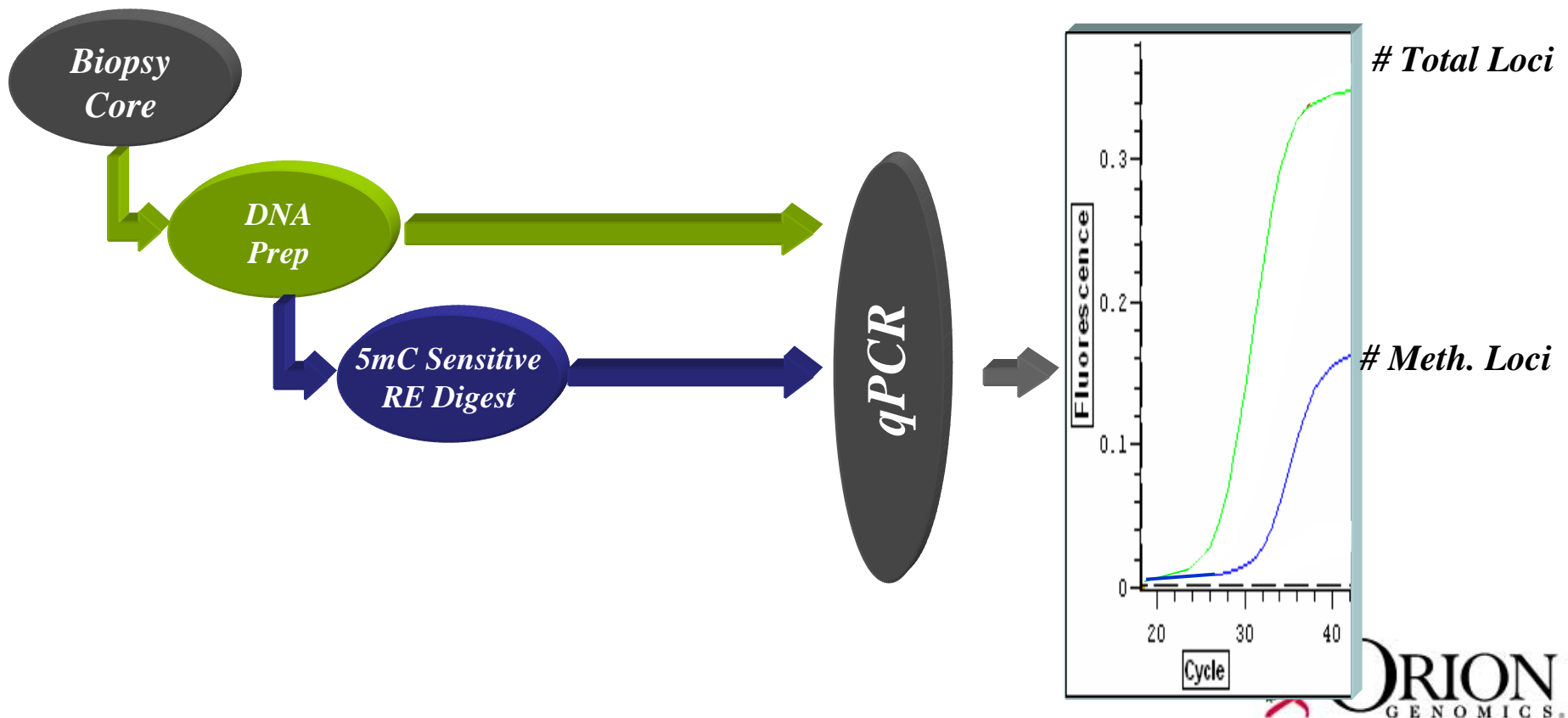




# MethylScreen™ Assay: Overview

A straight forward assay:

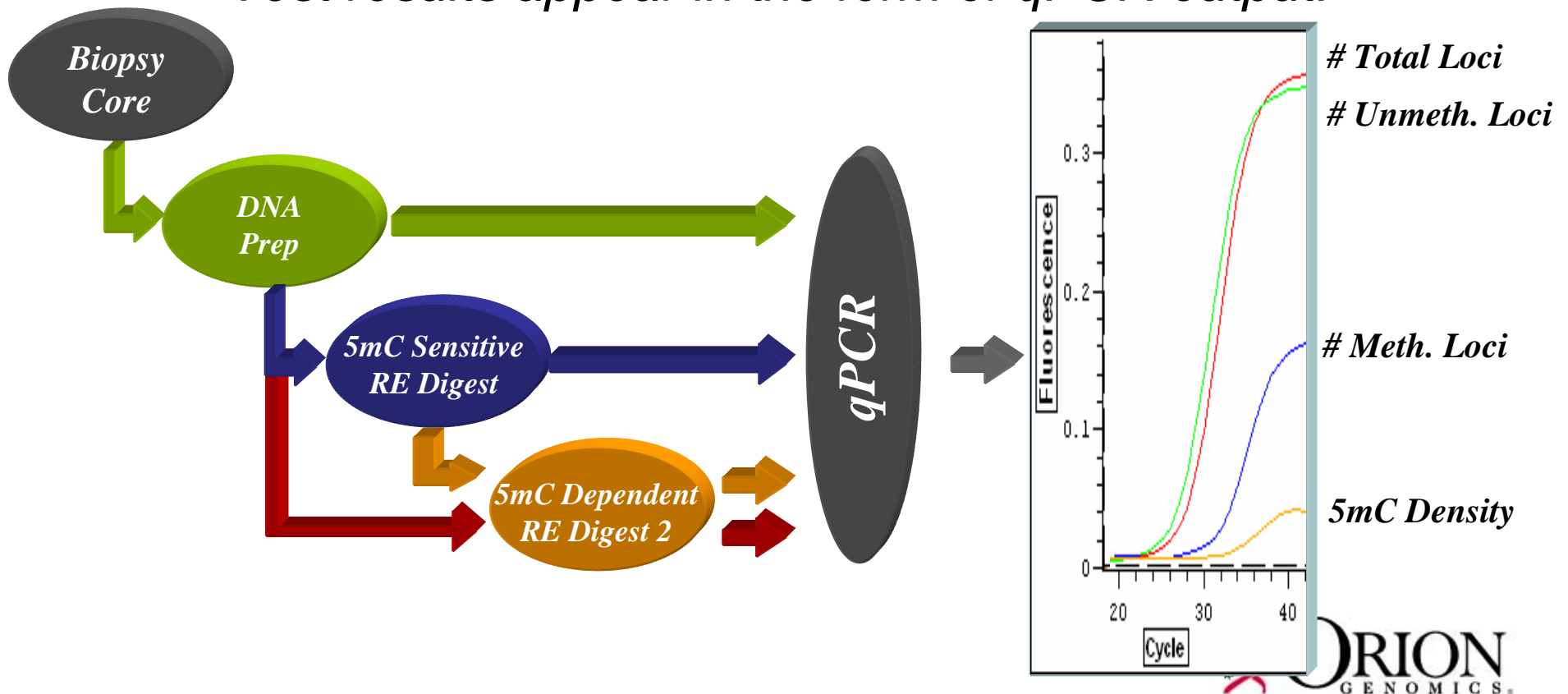
- *Normal DNA is digested away with reliable methylation sensitive restriction enzymes...*



# MethylScreen™ Assay: Overview

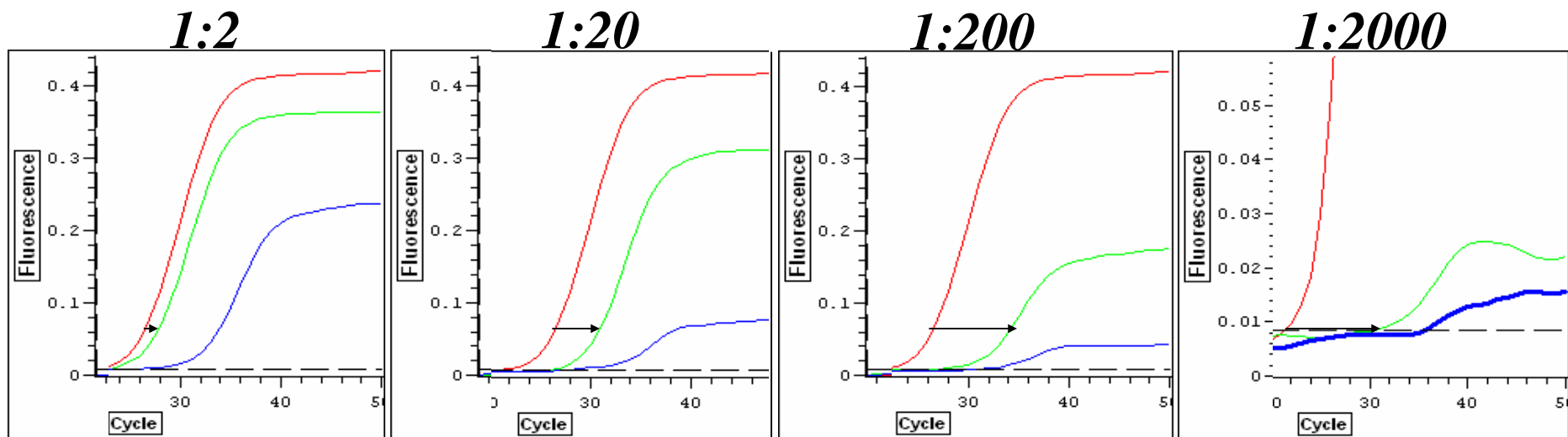
A straightforward assay:

- *Remaining disease DNA is partially degraded with a methylation dependent restriction enzymes.*
- *Test results appear in the form of qPCR output.*



# Demonstrating the Sensitivity of MethylScreen™ Technology

*Densely methylated gDNA diluted into unmet gDNA*



$\bar{X}$   $\Delta Ct = 0.9$   
 $E = 1$

$\Delta Ct = 3.9$   
 $E = \sim 3.3$

$\Delta Ct = 6.7$   
 $E = \sim 6.6$

$\Delta Ct = 11$   
 $E = \sim 10$

$2^{\bar{X}} = 10$  fold,  $\bar{X} = 3.33$   
( $n = 2/\text{dilution}$ )

■ - *HhaI*(total DNA)  
■ + *HhaI* (5mC DNA)  
■ + *HhaI* + McrBC

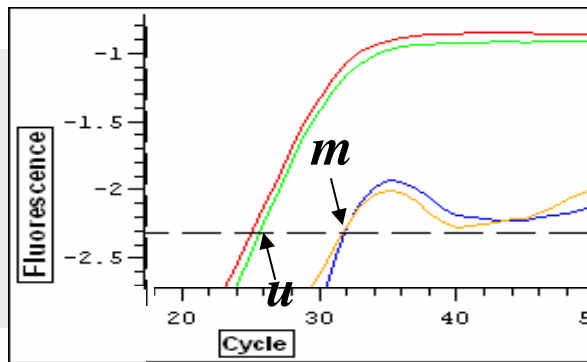
MS RE removes unmethylated DNA as predicted



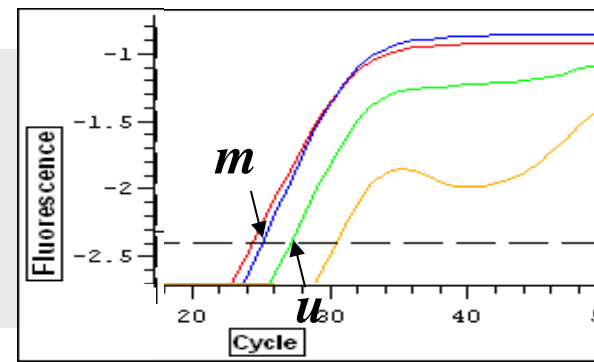
# MethylScreen Technology

*Prostate  
Tissue*

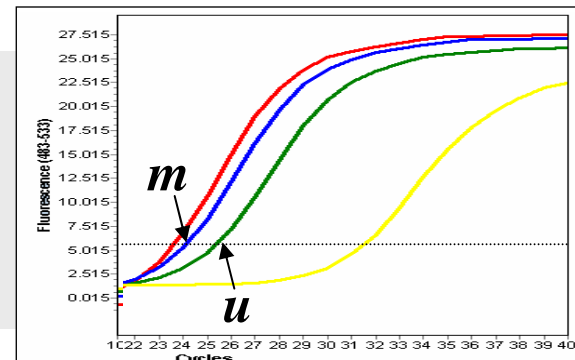
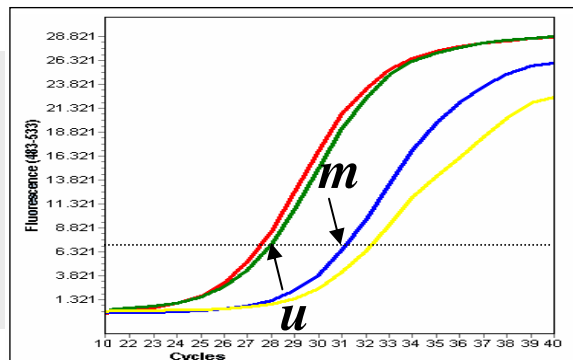
*Normal*



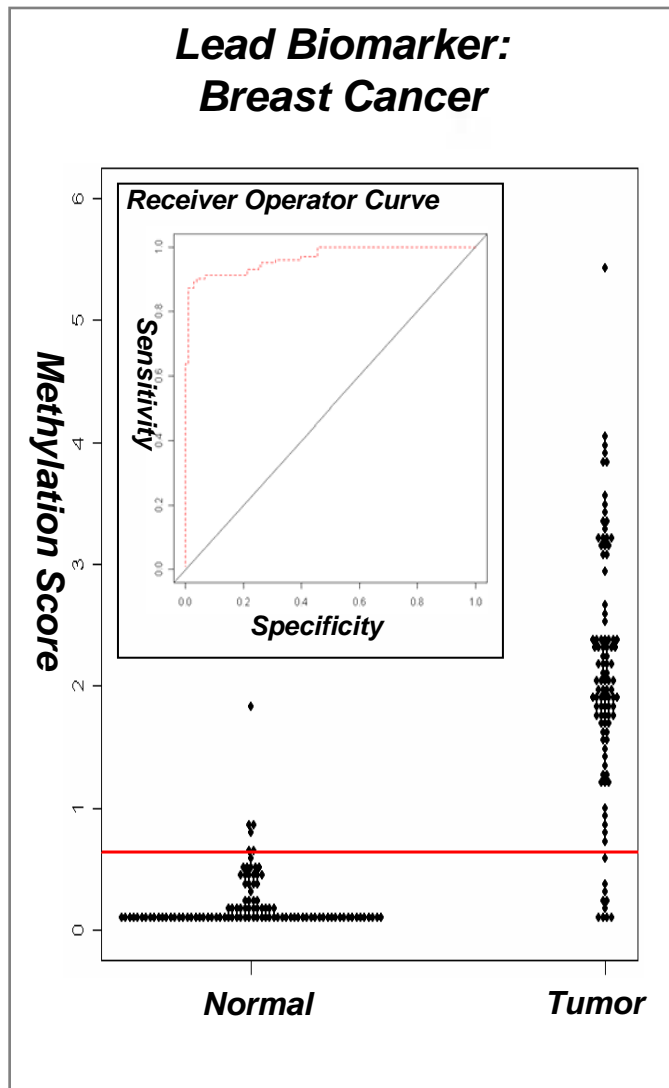
*Tumor*



*Breast  
Tissue*



# Lead Breast Cancer Biomarker

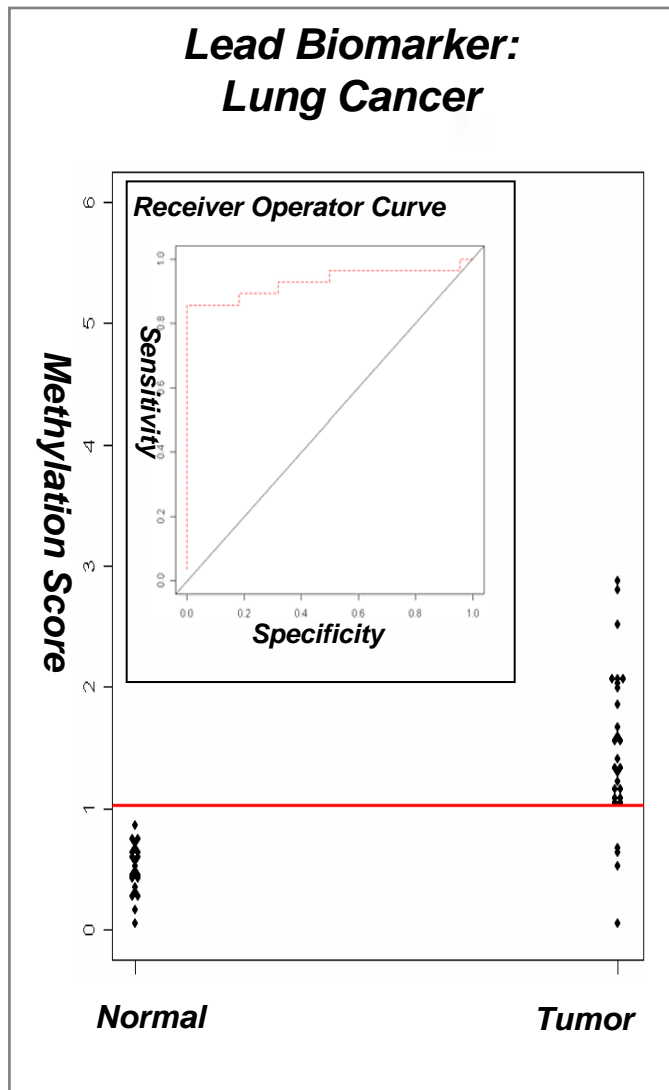


53 validated breast cancer biomarkers

Lead biomarker:

- Tissue samples from 205 patients
- 90% sensitivity (92/102 tumor)
- 96% specificity (99/103 normal)

# Lead Lung Cancer Biomarker

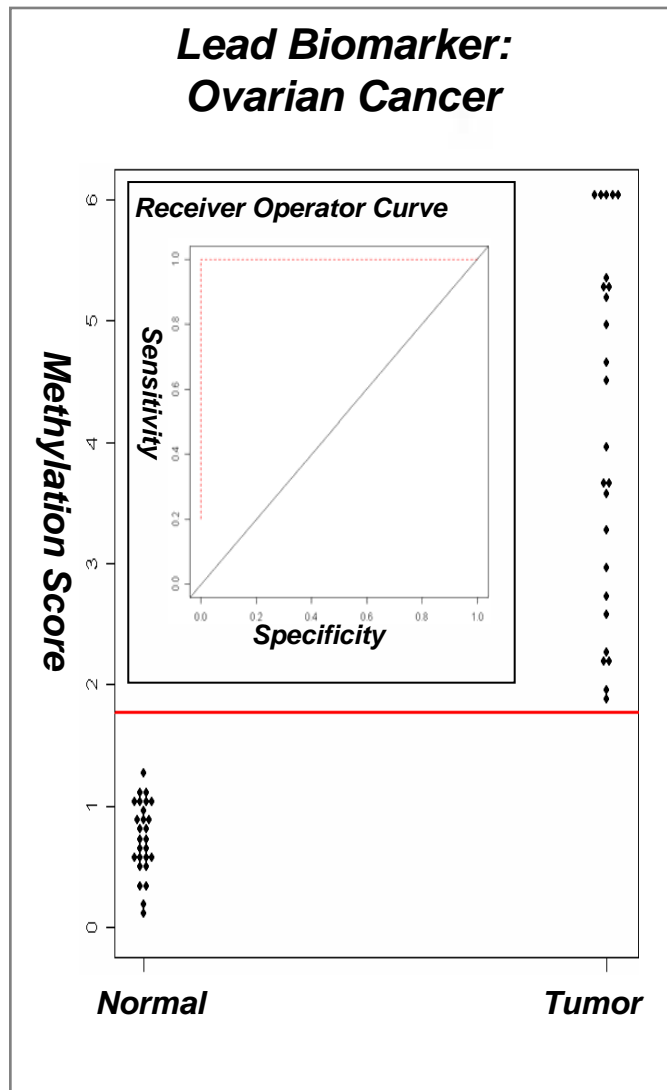


49 validated lung cancer biomarkers to date

*Lead Biomarker:*

- Tissue from 50 patients
- 86% sensitivity (24/28 tumor)
- 100% specificity (22/22 normal)

# Lead Ovarian Cancer Biomarker



46 validated ovarian cancer biomarkers to date...

*Lead Biomarker:*

- *Tissues from 52 patients*
- *100% sensitivity (25/25 tumor)*
- *100% specificity (27/27 normal)*

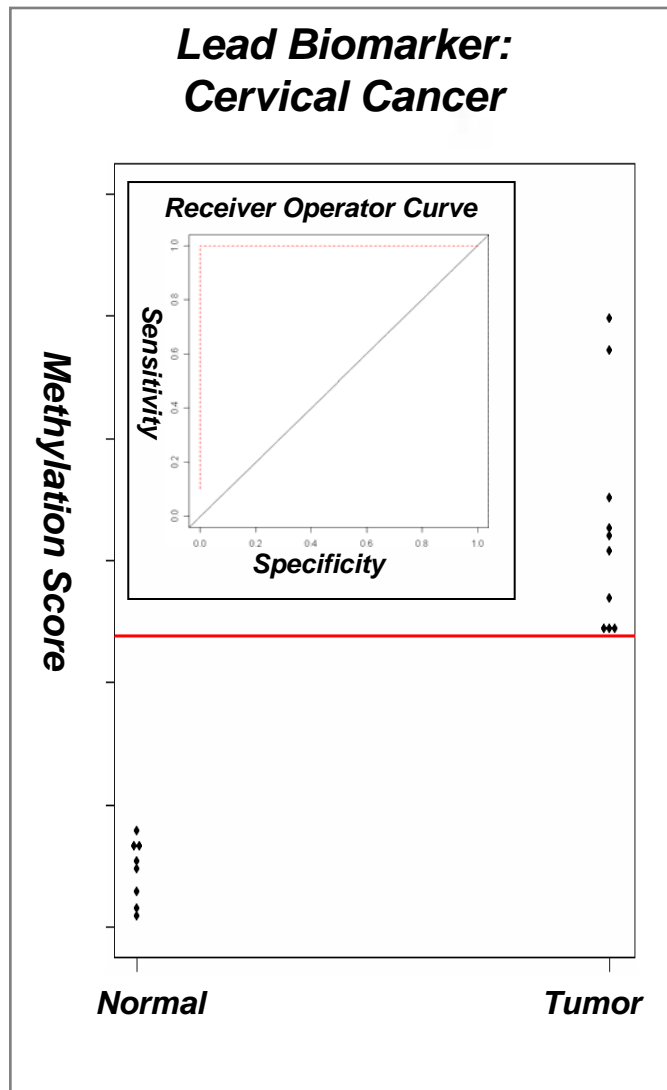


# Cross Tumor Validation

	Breast Cancer Program	Lung Cancer Program	Ovarian Cancer Program	Glioma Pilot
	53 biomarkers	49 biomarkers	46 biomarkers	
Breast				
Lung				
Ovarian				
Glioma				
Bladder				
Cervical				
Colorectal				
Endometrial				
Esophageal				
Head/ neck				
Leukemia				
Liver				
Melanoma				
Pancreatic				
Prostate				
Renal				
Thyroid				
Whole Blood				

- Collaboration with Mayo Clinic
- Biomarker Validation in 17 most common cancers
- 26 cervical cancer biomarkers found...

# Lead Cervical Cancer Biomarker



*26 validated cervical cancer biomarkers to date...*

*Lead Biomarker:*

- *Tissues from 18 patients*
- *100% sensitivity (10/10 tumor)*
- *100% specificity (8/8 normal)*

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